

TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference HP264	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2004/017490	International filing date (<i>day/month/year</i>) 25.11.2004	Priority date (<i>day/month/year</i>) 25.11.2003
International Patent Classification (IPC) or national classification and IPC A61K31/675, A61P7/10, 9/00, 9/04, 9/06, 9/10, 13/12, 25/04, 25/08, 29/00, 43/00		
Applicant NISSAN CHEMICAL INDUSTRIES, LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>9</u> sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input checked="" type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the claims:
- nos. _____ as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* _____ received by this Authority on _____
- nos.* _____ received by this Authority on _____
- ☐ the drawings:
- sheets _____ as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 18

because:

☒ the said international application, or the said claims Nos. 18
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matter of claim 18 pertains to
methods of treatment of the human body by surgery
and/or therapy, and diagnostic methods.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 18

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	8-10	YES
	Claims	1-7, 11-17, 19	NO
Inventive step (IS)	Claims	8-10	YES
	Claims	1-7, 11-17, 19	NO
Industrial applicability (IA)	Claims	1-17, 19	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
Document 1: WO 03/062201 A1 (VITTAL MALLYA SCIENTIFIC RESEARCH FOUNDATION), 31 July 2003			
Document 2: Kenji HARADA, "Clinical Efficacy of Efonidipine Hydrochloride, a T-type Calcium Channel Inhibitor, on Sympathetic Activities", Circulation Journal, 2003, Vol. 67, Issue 2, Pages 139 to 145			
Document 3: P. PHANI KUMAR, "Synthesis and Evaluation of a New Class of Nifedipine Analogs with T-Type Calcium Channel Blocking Activity", Molecular Pharmacology, 2002, Vol. 61, No. 3, pages 649 to 658			
Document 4: JP 60-69089 A (Nissan Chemical Industries, Ltd.), 19 April 1985			
Document 5: JP 63-233992 A (Nissan Chemical Industries, Ltd.), 29 September 1988			
Document 6: JP 1-275591 A (Nissan Chemical Industries, Ltd.), 6 November 1989			
Document 7: Hiromichi SUZUKI, "Cilnidipine no Jinkokasho wo Tomonau Koketsuatsu Kanja no Koatsu oyobi Nyotanpaku Gensho Koka", Therapeutic Research, 2000, Vol. 21, No. 4, pages 760 to 762			

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<p>Document 8: D. Bilici, "Protective Effect of T-type Calcium Channel Blocker in Histamine-induced Paw Inflammation in Rat", Pharmacological Research, 2001, Vol. 44, No. 6, pages 527 to 531</p> <p>Document 9: Chris Baylis, "Comparison of L-Type and Mixed L-and T-Type Calcium Channel Blockers on Kidney Injury Caused by Deoxycorticosterone-Salt Hypertension in Rats", American Journal of Kidney Diseases, 2001, Vol. 38, No. 6, pages 1292 to 1297</p> <p>Document 10: William F. McCalmont, "Design, synthesis, and biological evaluation of novel T-Type calcium channel antagonists", Bioorganic & Medicinal Chemistry Letters, 2004, Vol. 14, No. 14, pages 3691 to 3695</p> <p>Document 11: Darrell M. Porcello, "Actions of U-92032, a T-Type Ca²⁺ Channel Antagonist, Support a Functional Linkage Between I₊ and Slow Intrathalamic Rhythms", J Neurophysiol., 2003, Vol. 89, No. 1, pages 177 to 185</p> <p>(i) The invention set forth in claims 1 to 4, 11 to 17 and 19 lacks novelty and does not involve an inventive step in the light of document 1 cited in the international search report.</p> <p>Document 1 indicates that compounds represented by formulae I and II inhibit T-type calcium channels, and that said compounds are useful in the treatment of disorders related to calcium channel inhibiting activity (claims 1 to 54 and embodiment 18).</p>

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	<p>(ii) The invention set forth in claims 1, 5 to 7, 15 to 17 and 19 lacks novelty and does not involve an inventive step in the light of document 2 cited in the international search report.</p> <p>Document 2 indicates that Efonidipine inhibits T-type calcium channels, and that Efonidipine is useful in the treatment of hypertension, angina and the like (Abstract).</p> <p>(iii) The invention set forth in claims 1 and 11 to 14 lacks novelty and does not involve an inventive step in the light of document 3 cited in the international search report.</p> <p>Document 3 sets forth PPK17, PPK18 and the like, and indicates that said compounds hinder T-type calcium channels (Abstract, Table 1).</p> <p>(iv) The invention set forth in claims 15 to 17 and 19 lacks novelty and does not involve an inventive step in the light of document 4 cited in the international search report.</p> <p>Documents 4 to 6 indicate that compounds represented by the general formula (I) suppress the contraction of smooth muscle and cardiac muscle, and are effective in the treatment of coronary disorders, angina, hypertension and the like (see document 4, claim 1 and page 5, upper left column, lines 12 to 14; document 5, claims 1 to 5 and page 2, upper right column, lines 8 to 6 from the bottom; document 6, claims 1 to 8 and page 2, upper left column, lines 10 to 14). Moreover, document 7 indicates that cilnidipine lowers systolic blood pressure and diastolic blood pressure in patients with hypertension</p>

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

resulting from nephrosclerosis (see "Introduction" and "2. Results and Discussion").

(v) The invention set forth in claims 15 to 17 and 19 does not involve an inventive step in the light of documents 1 to 3 and 8 to 11 cited in the international search report.

Document 8 indicates that a T-type calcium channel inhibitor is useful in the treatment of inflammation, renal damage, cancer, epilepsy and the like (documents 8 to 11, Abstract).

It would therefore be easy for a person skilled in the art to conceive of applying the compounds set forth in documents 1 to 3, which have a T-type calcium channel inhibiting activity, to the treatment of inflammation, renal damage, cancer, epilepsy and the like, and doing so would not result in a special effect.

(vi) The invention set forth in claims 8 to 10 is not disclosed in any of the documents cited in the international search report, and is therefore novel and involves an inventive step. In particular, none of documents 1 to 11 which are understood to be the documents most closely related to the present application, indicate that of the compounds represented by formula (1), compounds wherein the nitrogen-containing heterocycle portion is a pyridine ring and Z is a group represented by formula (2) have a T-type calcium channel inhibiting activity.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 2004/024153 A2	25.03.2004	11.09.2003	12.09.2002
[E, X]			

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)
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